REMARKS

Claims 1, 2, 4, 5, 8, 9, 24, 25, 30, 34, 35, 37-40 and 43 are rejected. Claims 1, 24 and 30 are amended to recite the regulated removal of skin, supported at least in the Abstract. Applicant's counsel and technical advisor appreciate the courtesy of the July 1, 2005 telephone interview. The claims and references cited by the Examiner were discussed.

Applicant respectfully requests consideration of the following arguments which applicant believes puts the application in complete condition for allowance.

CLAIM REJECTIONS 35 U.S.C. §102

Claims 1-2, 4-5, 9-10, 24-25, 30-31, and 34-40 are rejected under 35 U.S.C. §102(b) as anticipated by SU1685448, maintained in the May 27, 2005 Advisory Action.

SU1685448 discloses a medicinal agent containing five ingredients: theophylline, trypsin, lanoline, sunflower oil, and dimethylsulfoxide (DMSO). In view of Krzysik and Harris, the Examiner's position is that trypsin is an inflammatory agent when applied to skin. In addition, in view of Schoer, Lapinet, and Bissett, the Examiner's position is that theophylline is an anti-inflammatory agent that decreases inflammation to the skin. Hence, "it can reasonably conclude that theophylline has no material effect on the activity of trypsin". Applicant submits a Declaration under 37 C.F.R. 1.132 analyzing why this is not a reasonable conclusion, and citing references in support of applicant's position that one skilled in the art recognizes that these agents do affect the material

function of the enzyme. For at least these additional references supporting applicant's position, applicant respectfully asserts SU1685448 does not anticipate the claimed invention, and requests its withdrawal.

Claims 1-2, 4-5, 9-10, 24-25, 30-31, 34-37, and 39-40 are rejected under 35 U.S.C. §102(b) as anticipated by de Faire, maintained in the May 27, 2005 Advisory Action.

The attached §1.132 Declaration analyzes how the claimed invention selectively regulates removal of a layer of skin and why deFaire's multifunctional enzyme cannot do so.

Applicant has also amended claims 1, 24, and 30 to clarify that the method regulates removal of a layer skin. Applicant's method is selective in that the physician can control, i.e., regulate, the removal of skin layer by the choice of enzyme, the type of administration of the enzyme (topical, injection, etc.), the amount of enzyme in the formulation, and the duration of treatment. For example, as described on page 17, lines 1-5 of the specification, low concentrations of enzyme are used to affect only epidermal layers of the skin whereas higher concentrations and/or a different formulation will affect not only epidermal but also the dermal layer of skin. It is the choice of enzyme, the concentration applied, the type of formulation applied, etc. that provide the user the means to target a layer of skin.

In addition, these parameters also regulate the depth of skin treatment. As described in the specification on page 17, lines 16-24; from page

19, line 22 to page 20, line 3; and from page 20, line 18 to page 21, line 13, proteases may be used to treat the outer layers of the skin, but when combined with other hydrolases, such as collagenases, proteases treat deeper layers. Thus, a protein with two distinct enzymatic activities (i.e., a multifunctional enzyme), even if it could be used in the claimed method (e.g., by treating it to inhibit other than the desired enzymatic activity) certainly cannot anticipate the claimed invention. In addition, the combination of enzymatic activities in a multifunctional enzyme may alter distinct and predictable properties of the separate enzymes, rendering any method using a multifunctional enzyme unable to regulate removal of a layer of skin.

CLAIM REJECTIONS 35 U.S.C. §§102, 103

Claims 1-2, 4-5, 9-10, 24-25, 30-31, and 34-40 are rejected under 35 U.S.C. §102(e) as anticipated by, or under 35 U.S.C. §103(a) as obvious over, Freeman, maintained in the May 27, 2005 Advisory Action.

In addition to applicant's previous analysis distinguishing Freeman, a §1.132 Declaration is attached, further demonstrating how Freeman neither anticipates nor renders obvious applicant's invention, and why one skilled in the art would not find Freeman doing so.

Freeman uses mechanical stripping. This is a destructive method. In contrast, applicant's claimed method allows reproducible, biologically predictable, and regulated, or selective, removal of layers of affected skin.

It is the Examiner's position to use the "broadest reasonable interpretation of the term topical application in the claim includes the treatment of

the Freeman document because the enzyme is brought in contact with the skin portion by directing the enzyme topically to the skin surface." Applicant respectfully disagrees because applicant's disclosure teaches away from this interpretation.

Freeman's invention uses a device that provides a continuous flow of the enzyme solution to contact the surface of the skin. The solution is delivered to the skin surface with sufficient force to effect a mechanical, "stripping" action. In addition to the enzymatic digestion of matrix proteins, the novel combination of a directional, mechanical force and enzymatic disruption of the lesion tissue enables the removal of cells from the treated surfaces (Freeman ¶0073).

Applicant, however, specifically state the following, which clearly contradict the Examiner's interpretation:

> Conventional skin destructive methods, such as topical application of liquid nitrogen and trichloroacetic acid, destroy tissue indiscriminately. The depth of tissue damage caused by these agents is a function of exposure time and/or concentration of the active agent. Conceivably, these conventional agents, if used in a sufficient concentration and for a sufficient exposure duration, would destroy not only full-thickness skin, but could produce damage extending into the deeper soft tissue and even bone. In contrast to conventional destructive agents, the inventive enzyme-containing compositions have the ability to produce selective tissue destruction limited to one or more layers of the skin, such as epidermis. For example, when the composition contains a protease and is topically applied, the enzyme may spread along the skin surface where it can interact with and destroy the epidermis only, or the epidermis and a portion of the dermis, or full-thickness skin. The skin layers affected can be altered by changing the

particular enzyme(s). The depth of skin affected can also be altered by changing the enzyme formulation, enzyme concentration, and/or exposure duration.

(instant specification page 19, beginning at line 13, emphasis added).

Applicant thus submits the invention is not disclosed by Freeman, at least because the claimed invention does not include directional and mechanical force, the "streaming of a solution", as Freeman requires. Applicant submits the invention is not rendered obvious by Freeman, because Freeman does not teach, motivate, or suggest that use of an enzyme alone without Freeman's device to effect mechanical stripping in addition to enzyme activity. Therefore, Applicant requests that the rejections over Freeman be withdrawn.

For the above reasons, applicant submits that the application in condition for allowance.

CONCLUSION

Applicant does not believe that there is any fee due with this submission. However, if any fees are necessary the Commissioner may consider this to be a request for such and charge any required fees to Deposit Account No. 23-3000.

The Examiner is invited to contact applicant's undersigned representative with any issues or questions.

Respectfully submitted,

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